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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/576,142 | 12/06/2006 | Thomas Arendt | 4121-180 | 5650 |

23448 7590 05/15/2009

INTELLECTUAL PROPERTY / TECHNOLOGY LAW
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| EXAMINER | |
|---|---|
| MACFARLANE, STACEY NEE | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1649 | |

| MAIL DATE | DELIVERY MODE |
|---|---|
| 05/15/2009 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/576,142 | ARENDT ET AL. | |
| | Examiner | Art Unit | |
| | STACEY MACFARLANE | 1649 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *29 January 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) *9-13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Response to Amendment*

1. Claims 1, 5, 8 and 13 have been amended as requested in the amendment filed on January 29, 2009. Following the amendment, claims 1-13 are pending in the instant application.

Claims 9-13 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper filed on May 29, 2008.

Claims 1-8 are under examination in the instant office action.

2. Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

3. Applicant's arguments filed on January 29, 2009 have been fully considered but they are not deemed to be persuasive for the reasons set forth below.

### *Claim Objections*

4. Claim 1 is objected to because of the following informalities: There is a misspelling in step (e) where the claim reads upon the quotient of the number of "calls". Appropriate correction is required.

### *Claim Rejections - 35 USC § 112*

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. As currently amended, Claims 1, 2 and 4-8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 recites "one or more mitogenically stimulated surface markers". Claims 2 and 4-8 are dependent from Claim 1 and do not further limit the "mitogenically stimulated surface markers", and are therefore included in the rejection. The claims do not require that the "mitogenically stimulated surface markers" possess any particular conserved structure or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of molecules that is defined merely by function (mitogenically stimulated to be expressed?) and the instant specification fails to describe the entire genus of molecules that are encompassed by these claims.

In making a determination of whether the application complies with the written description requirement of 35 U.S.C. 112, first paragraph, it is necessary to understand what Applicant has possession of and what Applicant is claiming. From the specification, it is clear that Applicant is in possession of specific examples of cell surface markers (page 4, paragraph 4). The claims, however, encompass a method of diagnosing Alzheimer's disease comprising quantification of mitogenically stimulated surface markers, thus, the claims are not limited to specific molecules with known

structure. The claims merely require the claimed methods employ molecules that are upregulated upon mitogenic stimulation, therefore, they are drawn to a genus of molecule, including markers as yet unknown, and there is inadequate description within the disclosure as to the entire genus of molecules encompassed.

In order to provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In the instant case, the only factor present in the claim is a recitation of activity. There is not even identification of any particular portion of a structure that must be conserved for said activity. As stated above, it is not even clear what molecules are considered mitogenically stimulated surface markers except those explicitly listed (page 4). The specification does not provide a partial or complete structure of any marker and fails to provide a representative number of species for the recited genus. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

*Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111, the court clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The

specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the molecules within the encompassed genus of "mitogenically stimulated surface markers", and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of identifying activity. Adequate written description requires more than a mere recitation of activity as part of the invention and a reference to a potential method of isolating or screening that fulfill said activity. The compound itself is required. See *Fiers v Revel*, 25 USPQ2d 1601 at 1601 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification only provided for the bovine sequence. Such is the case here, where Applicant has provided only for a specific subset of molecules and has not proved description for the broad class of mitogenically stimulated markers.

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. § 112 is severable from its enablement provision (see page 1115).

7. Claims 1-8 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method comprising obtaining patient samples

and quantifying the cells comprising cell surface antigens via immunodetection before and after mitogen stimulation, does not reasonably provide enablement for the detection of Alzheimer's disease wherein the relative number of cells is at least 10 times the unstimulated control. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The claims are draw to a method of diagnosing Alzheimer's disease or an early stage of or a predisposition for this disease comprising obtaining a patient sample of peripheral cells, quantifying the cells with respect to one or more surface markers, stimulating the cells with mitogen(s), quantifying the cells with respect the one or more surface markers post-stimulation, and calculating a stimulation index as the quotient of cells before stimulation and after, and detecting that the sample is from a patient suffering from AD or an early stage of or a predisposition for the disease if the stimulation index is at least 10 with a maximum of 100.

With respect to the disclosure the specification merely states: "A stimulation index which reaches at least 10 times, as a maximum 100 times, the unstimulated control sample, is a sign of an Alzheimer's disease or an early stage of or a predisposition for this disease. A stimulation index which is less than 10 times the unstimulated control sample is no sign of an Alzheimer's disease or an early stage of or a predisposition for this disease." There is no further direction within the disclosure for the method as currently claimed. This is the only guidance provided within the specification as to how one of ordinary skill is to perform the method requiring Claim 1

part (f), and this, in an of itself, teaches away from the claimed method, as it states that a stimulation index which is less than 10 times the unstimulated control sample may be an indication of the disease at the early stage or a predisposition for the disease encompassed by the claims. Thus, the guidance within the disclosure is merely speculative and postulates how the invention may work but does not provide guidance to one of ordinary skill in the art that the method can be performed with a reasonable expectation of success of diagnosing of Alzheimer's disease. Therefore, the specification is not enabling commensurate in scope with the claims.

Prior to filing, methods comprising stimulation of peripheral lymphocytes with the instantly-elected PWM, quantification of the cells by cell sorting using the surface marker CD69 and further specifying and separating cells as CD4+ and/or CD8+ subpopulations via flow cytometry using monoclonal antibodies were well known in the art (Neubert et al., 2000, cited in previous Office action mailed 7/31/2008). It was also well-recognized that the method could be practiced using samples from patients with Alzheimer's disease with respect to "potentially diagnostic purposes" (Stieler et al. 2001, and cited as reference AF on the IDS filed 9/5/2006). The Stieler et al. reference teaches a method comprising the active steps of stimulating a citrate stabilized blood samples of lymphocytes with PWM, quantifying the cells by cell sorting using the surface marker CD69 and further specifying and separating cells as CD4+ and/or CD8+ subpopulations via FACScan-analysis. Stieler et al. also teaches the effects of mitogenic stimulation as a function of the number of cells bearing the surface marker(s) before and after stimulation or as a "stimulation index" and correlates that to ApoE

genotype. However, there was nothing of record to suggest that a definitive diagnosis of Alzheimer's disease or early stage or predisposition for disease could be determined wherein the stimulation index was at least 10.

The standard of an enabling disclosure is not the ability to make and test if the invention works but one of the ability to make and use with a reasonable expectation of success. A patent is granted for a completed invention, not the general suggestion of an idea and how that idea might be developed into the claimed invention. In the decision of *Genentech, Inc, v. Novo Nordisk*, 42 USPQ 2d 1001, (CAFC 1997), the court held that:

> "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable" and that "[t]ossing out the mere germ of an idea does not constitute enabling disclosure". The court further stated that "when there is no disclosure of any specific starting material or of any of the conditions under which a process is to be carried out, undue experimentation is required; there is a failure to meet the enablement requirements that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art", "[i]t is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement".

Examiner concludes that the instant specification is not enabling because a skilled artisan cannot follow the guidance presented therein and practice the claimed method without first making a substantial inventive contribution. In the instant case, one

of ordinary skill in the art would have to demonstrate that the method wherein the stimulation index of at least 10 for any mitogenic surface marker upon stimulation with any mitogenic factor is indicative of a definitive diagnosis of Alzheimer's in order to practice the method as claimed. Such experimentation is not routine but constitutes undue experimentation in order to close the gaps between laboratory data and clinical application. Therefore, the claims are rejected.

***Conclusion***

8. No Claim is allowed.

9. This application contains claims drawn to an invention nonelected with traverse in Paper filed on May 29, 2008. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to STACEY MACFARLANE whose telephone number is (571)270-3057. The examiner can normally be reached on M-W and ALT F 5:30 to 3:30, TELEWORK-Thursdays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Stacey MacFarlane
Examiner
Art Unit 1649

/John D. Ulm/

Primary Examiner, Art Unit 1649